Hyperosmotic stress-dependent NF?B activation is regulated by reactive oxygen species and IGF-1 in cultured cardiomyocytes

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We have recently shown that hyperosmotic stress activates p65/RelB NF?B in cultured cardiomyocytes with dichotomic actions on caspase activation and cell death. It remains unexplored how NF?B is regulated in cultured rat cardiomyocytes exposed to hyperosmotic stress. We study here: (a) if hyperosmotic stress triggers reactive oxygen species (ROS) generation and in turn whether they regulate NF?B and (b) if insulin-like growth factor-1 (IGF-1) modulates ROS production and NF?B activation in hyperosmotically-stressed cardiomyocytes. The results showed that hyperosmotic stress generated ROS in cultured cardiac myocytes, in particular the hydroxyl and superoxide species, which were inhibited by N-acetylcysteine (NAC). Hyperosmotic stress-induced NF?B activation as determined by I?B? degradation and NF?B DNA binding. NF?B activation and procaspase-3 and -9 fragmentation were prevented by NAC and IGF-1. However, this growth factor did not decrease ROS generation induced by hyperosmotic stres